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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HELMER, GEORGIA L	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 07/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/997,445	XUE ET AL.	
	Examiner	Art Unit	
	Georgia L. Helmer	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date ~~16 June 2004~~.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1-11 are pending and are examined in the instant action.

Information Disclosure Statement

2. Applicant's IDS filed 18 April 2002 is acknowledged and a signed copy included herewith.

Priority

3. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in the China, 00131217.0, filed 03 December 2000. Applicant has filed a certified copy of the priority document, EP99114074.0 application as required by 35 U.S.C. 119(b). In order to perfect foreign priority, Applicant can submit an English translation of the priority document.

Claim Rejections - 35 USC § 101

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claim 11 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 11 is drawn to a "use" which is not one of the five statutory classes of patentable subject matter.

Claim Rejections - 35 USC § 112-2

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 6 is rejected under 35 USC § 112-2 for the following reasons:

In claim 6 (a) recites "the transformation techniques" which phrase lacks antecedent basis. All dependent claims of claim 6 are also rejected.

Corrections or clarifications are required.

Claim Rejections - 35 USC § 112 Enablement

8. Following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is considered in view of the *Wands* factors (MPEP 2164.01(a)).

The breadth of the claims: The claims are drawn to a transgenic Dunaliella Salina (a single-cell photosynthetic algae) comprising a Dunaliella Salina as host, a foreign target gene and a selectable marker; a foreign target gene derived from

humans, animal, plants or microorganisms, where the target gene is derived from HBsAg, measles virus antigen foot-and –mouth virus antigen, rabies virus antigen, larvacide, cytokinin, endochitinase, gluocse-amylose P, thaumatin, seed-stored proteins genes; where the foreign target gene is derived from humans and animals and is unspecified or comprises virtually all protein encoding genes, where the selectable marker is unspecified or comprises virtually all protein encoding genes conferring resistance to antibiotics or herbicides. The claims are also drawn to a method of preparing a transgenic Dunaliella Salina bioreactor comprising introducing foreign target gene into Dunaliella Salina cells using unspecified or Agrobacterium transformation techniques, and screening transformed cells. The claims are further drawn to the use of a transgenic Dunaliella Salina bioreactor to produce drugs or vaccines or phytohormones, and to the Dunaliella Salina bioreactor produced, The claims are drawn broadly to transient or stable transformation, of nuclear or chloroplast genomes, to all foreign target genes, all selectable markers and to all transformation techniques.

The state of the art and the unpredictability thereof. Plant transformation is unpredictable. According to Hansen, "[P]lant transformation is an art because of the unique culture conditions required for each crop species. To accommodate a genotype or species that has not been manipulated in culture previously, one must either adapt an established protocol or create a new one", (Hansen et. al., 1999, Trends in plant Science, Vol 4, pages 226-231, see page 230). Applicant has given no guidance or working examples of DNA introduction by particle bombardment or by microinjection.

Plant chloroplast transformation is unpredictable. Chasen (Plant Cell, Vol. 4, pages 1-2, 1992, p.) observed that in chloroplast transformation by homologous recombination using two selectable markers, while the selected marker was stably integrated, unselected markers segregated out in the next generation. This unpredictability suggested that recombination events may prevent integration of long segments of homologous DNA in plastics.

Guidance Applicant describes construction of an expression vector comprising a Dunaliella Salina Hsp70B 5'promoter and a hepatitis B antigen gene fusion with cholera toxin B (Specification, p. 14 line 6 bridging to p. 15 line 12), followed by introduction of this DNA into Dunaliella Salina cells via electroporation (specification, p. 11, line 13-29). Applicant does not describe the production of transgenic Dunaliella Salina, which function as a bioreactor.

Experimentation required: Undue experimentation would be required to determine which foreign gene, derived from what source—plants, microorganisms, animal and humans, whether using genomic DNA or using cDNA for the coding sequence, what 5' regulatory sequence(s) would function as desired, be they constitutive or regulatable, and whether they need chloroplast or nuclear transcription machinery, so that they can be put into the appropriate organellar or nuclear location; what suitable selection marker(s) to use—be they antibiotic resistance markers or herbicide resistance, the functionality of each differing also between the chloroplast and the nuclear genes because the selective agents (antibiotic or herbicide) have specific targets for activity. For selectable markers, experimentation to determine what antibiotic

agents, at what levels, in solid or liquid medium, would function as desired. Having made decisions based on these experiment parameters, experimentation would then be required how to introduce the DNA into the Dunaliella Salina—physical methods, such as electroporation or gene-gun, or biological methods such as Agrobacterium transformation, and whether the successful transformation be transient or stable. Another set of cascading experiments would be required to determine what foreign gene would function as desired for Dunaliella Salina functions to produce the desired product –are introns processed properly, does the gene have codon usage functional in Dunaliella Salina, is glycosylation proper since plant and animal glycosylation products differ, and is the product toxic to the transgenic Dunaliella Salina? This is a special problem if the Dunaliella Salina is used to produce phytohormones, as claimed—most phytohormones are not proteins and virtually all phytohormones are functional at very low level and are deleterious to plants at higher levels. Applicant must provide sufficient guidance to address these issues. Without such guidance the experimentation required would not be routine, but would be undue. This would impose a burden on the skilled artesian, without a reasonable expectation of success.

In view of the breadth of the claims (all foreign genes, derived from all animals, humans, plants and microorganisms, all selectable marker genes, all means of transformation including physical, chemical or biological methods, production of all drugs and vaccines and phytohormones), the nature of the invention, the unpredictability of the art, the lack of guidance in the specification, undue trial and error

experimentations would be required to enable the invention as commensurate in scope with the claims.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-7, 10 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Porath, et. al. (Developing a transformation system for Dunaliella, 1997, Phycologica, Vol 36, No 4 SUPPL, page 89, Meeting information: Sixth International Phycological Congress. Leiden August 9-16, 1997).

Porath et. al. teach a transgenic Dunaliella Salina (lines 10-12) comprising a Dunaliella Salina as host, a foreign target gene—the cbr gene of Dunaliella bardawil (lines 7-9) and a selectable marker—the ble gene of Chlamydomonas reinhardtii (lines 16-22); which is a foreign target gene derived from an algae (algae are plants), where the selectable marker is the ble gene which codes for phleomycin resistance (lines 23-24). Porath et. al. also teach a method of preparing a transgenic Dunaliella Salina bioreactor comprising introducing foreign target genes into Dunaliella Salina cells using an unspecified transformation technique (lines 11-12), and screening transformed cells for phleomycin resistance (lines 23-24). Porath et. al. also teach the use of the transgenic Dunaliella Salina bioreactor to produce a drug, the ble gene product (lines

23-24) which is an enzyme capable of metabolizing phleomycin, an antibiotic. Porath et. al. also teach the method comprising culturing Dunaliella Salina prior to introducing the foreign genes. It is a standard laboratory procedure for the host cells to be cultured (and in a growth phase) prior to inserting of foreign DNA; therefore preculturing is inherent in the method of Porath et. al.

Accordingly Porath et. al. anticipate the claimed invention.

Remarks

12. No claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Georgia L. Helmer whose telephone number is 571-272-0976. The examiner can normally be reached on 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 571-272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Georgia L. Helmer
Patent Examiner
Art Unit 1638
June 28, 2004

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